1

Introduction to Haptic Optical Tweezers

1.1. Introduction

Micro- and nanotechnologies are, in theory, very attractive. Theoretical models predict incredible properties for nano- and microstructures. In practice, however, researchers and inventors face an unknown puzzle: there is no analogy in the macroworld that can prepare operators for the unpredictability and delicacy of the microscopic world. Existing knowledge and know-how are experimentally insufficient. Exploration is the most delicate and unavoidable task for micromanipulation, microfabrication and microassembly processes. In biology, the manipulation and exploration of single cells or protein properties is a critical challenge [ZHA 08a, MEH 99]. This can only be performed by an experienced user. These procedures are highly time-consuming and uneconomical.

Well-designed user interfaces and force-feedback teleoperation increase the achievable complexity of operations and decrease their duration [HOK 06]. Several works have considered the coupling of existing micromanipulators to commercial or prototype haptic devices [SIT 03, KHA 09, WES 07] with little success. Indeed, the feedback is dependent on the degrees of freedom of the platform, the range of scaling and the type of interaction to render. Compared to other techniques, optical tweezers (OTs) [ASH 86] seem to be more promising for the integration of the robotic technique of force feedback teleoperation (see Figure 1.1). OTs are a very versatile tool and the quality of possible force feedbacks can be improved by the techniques discussed in this chapter. The chapter also highlights a new approach: to rethink the design of micromanipulators in order to reliably and usefully render the interaction through the user interface.

Figure 1.1. *Dextrous use of a micromanipulation platform. An optical trap is teleoperated with an interface that allows force measurement feedback to be haptically experienced. A 3D reconstruction of the scene can also increase user immersion. The haptic interface presented is the Omega^{TM} from Force Dimension. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

Appropriate techniques to get the user a high-quality force feedback with OTs are discussed. Better dexterity is achieved and tasks of higher complexity are performed with little knowledge and implementation of the haptic teleoperation methods. The principles for interactive micromanipulation systems and the advantageous properties of OTs are summarized in section 1.2. The different existing components and techniques of optical trapping are summarized and their drawbacks for haptic purposes are highlighted in section 1.3. As a consequence, new designs specific to haptic applications are discussed in detail in section 1.4, based on the most recent experiments described in the literature. Finally, the prospects brought by this new approach are carefully highlighted in section 1.5 in order to encourage further developments in this domain.

1.2. A dexterous experimental platform

Everyday interactions and manipulations are possible because of our remarkable sensors (our eyes and proprioceptive systems) and effectors (our hands and muscles). Traditional tools for visualizing and interacting with the microworld are not nimble or transparent. Microscopes and micromanipulators historically do not lend themselves to intuitive interaction or handling because human vision is two-dimensional (2D), force sensors are rare and the degrees of freedom are reduced. Intuitive interactions and control are especially complicated because of the particular phenomena of the microworld.

1.2.1. *A dexterous micromanipulation technique*

Micromanipulation experiments are often poorly repeatable, time-consuming and costly because of unique physical phenomena at this scale. Surface interactions become more significant than volume interactions for objects smaller than 500 μm. Particles tend to adhere and become bound to handling tools or substrates, or surface forces interact with low-inertia particles to produce huge accelerations which can damage or eject samples.

Properties	EM tweezers	Optical tweezers	AFM
Control	Individual	Individual	Individual
Tool	magnetic bead	dielectric bead	microtip
Tool size (μm)	$0.5 - 5$	< 20	$100 - 250$
Forces (pN)	$0.01 - 100$	$0.1 - 400$	$10 - 10^4$
Stiffness ($N.m^{-1}$)	10^{-7}	$10^{-7} - 10^{-3}$	$10^{-2} - 10^2$
Environment	Air and water	Water (mainly)	Air and water
Parallelism	1 trap	1 to 200 traps	1 or 2 tips

Table 1.1. *Comparison of three individual techniques of micromanipulation (based on molecular study applications [NEU 08])*

Many handling techniques have been designed to address the adhesion problem [CHA 10]. Current designs are focused on the development of miniaturized microtools with functionalized surfaces (atomic force microscope (AFM) probes [XIE 09], microgrippers [AND 09]) or potential field levitation and non-contact guiding (OTs [ASH 86], magnetics tweezers [GOS 02, VRI 05], electrophoresis [WAN 97], microfluidics [SQU 05], etc.).

In this chapter, we will only consider grasping phenomena that facilitate the manipulation of individual independent microscopic tools (electrophoretic, and microfluidics do not permit isolation of a single effector). AFM and microgrippers make possible independent displacement and application of high-amplitude forces ($10 - 10^4$pN). However, the effectors are large and therefore adhesion, inertia and visual obstruction limit their performance. Electromagnetic techniques have a localized magnetic field, but it is difficult to independently manipulate several robots [DIL 13]. Also, electromagnetic techniques can only be considered as an independent tool when the properties of the trap probe are very different from the sample nature, such as proteins, cells or non-magnetic microassembly parts.

OTs [ASH 86, NEU 04] avoid many of the limitations of competing techniques (see Table 1.1 for comparisons). Compared to other micromanipulation techniques, OTs offer greater versatility. Optical trapping relies on an immaterial electromagnetic field produced by highly focused laser light. This produces optical force (<100 pN) which is effective for the manipulation of particles between 100 microns [SHV 10] and atomic scale [ASH 00]. A highly focused laser produces a localized three-dimensional (3D) electromagnetic field that stably traps spherical dielectric microtools. This probe is then easily actuated by deflecting or defocusing the laser. The optical forces are easily modeled and 3D trap stiffness can be estimated experimentally [ROH 02, ASH 92, BER 04]. Particle tracking makes it possible for the force on the probe to be measured (see section 1.3.3). There are many experimental setups that use high-speed actuation (1 GHz bandwidth [RUH 11]) and high-precision force measurement (femtoNewton [ROH 05a]). Time or spatial sharing of the laser power also offers parallelisms the possibility of trapping: experiments have shown that more than 200 parallel traps [CUR 02] or up to 9 parallel sensors [SPE 09] have been accomplished on a single system. These properties of OTs, i.e. high speed, high precision and the capability for multiple independent interactive probes, allow unprecedented opportunities for teleoperative control of microscopic systems. The techniques for efficient construction of the force feedback interfaces are detailed in the next section.

1.2.2. *A dexterous user interaction for micromanipulation*

Force feedback teleoperation techniques originate from nuclear energy plants, where maintenance tasks can only be performed from a distance [SHE 92]. The aim of these techniques is to recreate the bilateral interaction between the user and an unreachable environment; in other words, touch sensations can be recovered on a system where the mechanical linkage is disconnected. In our case, microscopic particles are mechanically disconnected from the user's hands. Teleoperation techniques can be extended to micromanipulation platforms in the following way. A master robot, also called the active joystick or the haptic user interface, is connected to a slave robot (in our case, the OT platform):

– the position orders are recorded by the interface handle, scaled and used to command the microtool displacements;

– at the same time, the scaled forces that are measured in the microworld are fed back to the user through the motors of the active joystick.

This is a bilateral process, named the "haptic coupling loop" (see Figures 1.2(b) and (d)). The characteristics of this kind of automatic scheme are well known [LAW 93]. Stability and transparency are the main issues for an accurate bilateral transmission. Stable systems do not diverge from equilibrium positions. For bilateral coupling, this state can be evaluated by the sufficient condition of passivity: the ability of a system not to add energy in the loop [HAN 02]. Transparency can be defined as the degrees of reliability and latency of the transmission, which is measured by the frequency bandwidth of the system. It is important to note that human temporal frequency bandwidth is estimated up to 1 kHz for force perception and over 10 kHz for textures [JON 06]. This means that human hands are able to perceive discontinuity of the signal under this sampling limit. It is critical that the bandwidth and sampling of all components and coupling of the system are over those thresholds.

The most realistic force feedback is obtained with a scheme called direct coupling because it is only composed of fixed homothetic scaling gains (see Figure 1.2(d)) [BOL 09]. Unlike passive coupling (see Figure 1.2(b)), direct coupling does not possess a filter to reduce information reliability and response time. It, therefore, has great fidelity and is referred to as a transparent coupling. However, it is not unconditionally stable, and the stability must be carefully controlled for safe use [BOL 09].

Direct coupling is even worse in the case of micromanipulation because high scaling effects appear: position information is scaled from milli- to micrometers, and forces are scaled from imperceptible nanoNewton to the human perception thresholds [JON 06] (>0.01 N for fingers, >1 N for the hand). These huge scaling factors amplify the signal noise and measurement uncertainties, reducing system stability and the operator's understanding [BOL 09]. For example, a bilateral system including an AFM tip (see Figure 1.2(a)) requires additional damping components in order to maintain stability during transitions from contact to non-contact, due to adhesion [BOL 08] (see Figure 1.2(b)). Since damping factors strongly filter high frequencies, direct feedback of measurement is, in this case, not usable and an artificial enhanced metaphoric feedback must be designed instead [BOL 09, BOL 10].

Unlike AFM conditions, the force versus position curve of OTs (see Figures 1.2(c) and 1.2(d)) presents two significant advantages: the absence of hysteresis and the absence of discontinuities due to adhesion. Additionally, OTs act as a natural spring damping element which provides sufficient damping to maintain stability [PAC 09, PAC 10]. OTs, operating in an aqueous medium, have good stability and transparency properties with direct coupling (no energy dissipation, no filters needed). However, pioneering works [ARA 00] focused on other problems and did not emphasize this potential.

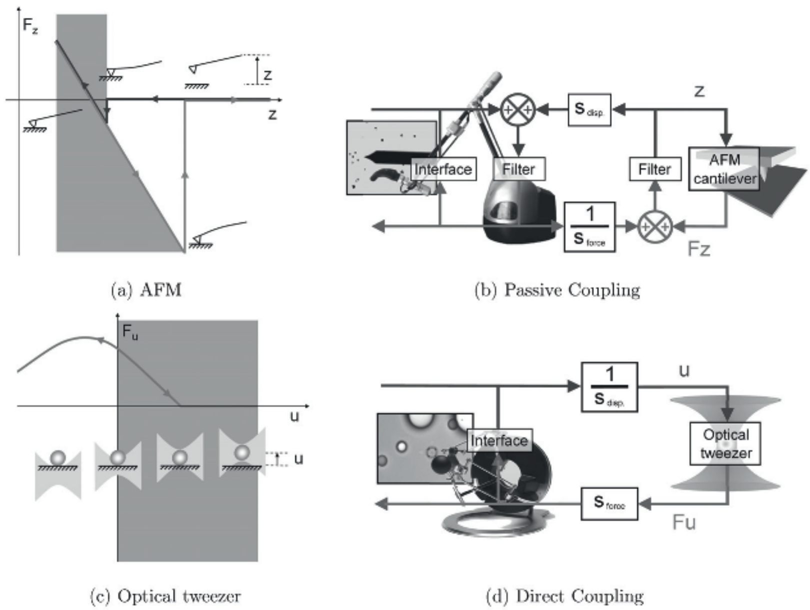


Figure 1.2. *Comparison of force measurement methods during an approach-retract task for AFM and OT. Force-position characteristics with high adhesion effects for an AFM sensor a) and the corresponding coupling scheme b). Force-position characteristic for an OT sensor c) and the corresponding coupling scheme d). "z" is the displacement of the AFM support and "u" is the laser displacement.* S_{disp} *and* S_{force} *denote the displacement and force scaling gains, respectively. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

1.2.3. *Pioneering works*

Vigorous activity in the OT community has been devoted to the improvement of the user interface, such as joysticks [GIB 07], hand tracking [WHY 06, MCD 13, SHA 13], multitouch table [GRI 09, BOW 11b], and haptic interface [ARA 00, BAS 07, BUK 08, PAC 09, PAC 10, BOW 11a, OND 12a]. Other works have reported connecting a haptic device to OTs without describing results or sensations [BER 09, LEE 07, SUG 08].

Arai *et al*. [ARA 00] achieved the first haptic coupling for OT in 2000 and also identified different limitations of the sensors used. Actuators and sensors limit either the system bandwidth or the working domain. At that time, the available cameras had slow frame rates (Charged-Coupled Device (CCD): 15 frames per second) and could not be included in a control loop. As a result, the actuator and sensor used (microscope stage and quadrant photodiode) limited the stability and transparency of this system, resulting in a low feedback amplitude (< 1 N).

Those technical limitations explain choices made by Basdogan *et al*., in 2007, in order to propose model-based feedback for guidance assistance [BAS 07, BUK 08]. By not having measurement and feedback of real forces, the system is not considered as bilateral and the stability issues are avoided. The virtual force feedback can then be increased on the handle with no consequences. With a 3D piezoelectric scanner and scene recognition techniques, this method allows us to avoid obstacles and perform efficient microsphere dockings.

Still, this guidance feedback is limited to simple and controlled scenes, and does not fulfil the need of preliminary explorations with real feedback. To obtain stable bilateral coupling, efforts must be focused on improving the performance of the optical experimental setup. For a useful force feedback teleoperation between a user and the microworld, the important parameters of the new design are the following:

– interactive mobility (workspace, degrees of freedom and measurement and parallelism);

– bandwidth (reactivity, dynamics of the system, fidelity of the information and transparency);

– feedback intensity (perceptible force amplitude, stability limitations, effective assistance and user safety).

1.3. Interactive optical tweezers

Interaction between two objects means the whole process of action and reaction. In teleoperated manipulation, an interactive system possesses actuators, sensors and a bilateral transmission to interact with the user. This section examines why, in OT platforms, the working domain of sensors is very small, when high-speed actuation is used [PAC 09, PAC 10]. It demonstrates the incompatibility of previous experimental workbenches for the sought performances of interaction involving high speed and dexterous working space. The right choice of the actuators and sensors is highly important for force feedback applications and is explained in detail.

1.3.1. *Displacement techniques*

Displacement in OT systems can be achieved by moving the platform or moving the laser beam, referred to hereafter as stage-based or laser-based actuations. In the stage-based techniques [SIM 96], the laser beam is fixed and an actuated stage facilitates the motion of the sample. The desired target comes to the laser spot (see Figures 1.3(a) and (b)). This trap is always aligned with the optical axis, which is very convenient for the force measurement. Their heavy mechanical parts state microscope stages as the slowest available actuation techniques. This configuration is convenient for high-quality force measurement like photonic force microscope [ROH 04], but not for the high speed control of the trap. Teleoperation techniques need high temporal bandwidth, which is why high-speed actuation techniques based on deflection must be used.

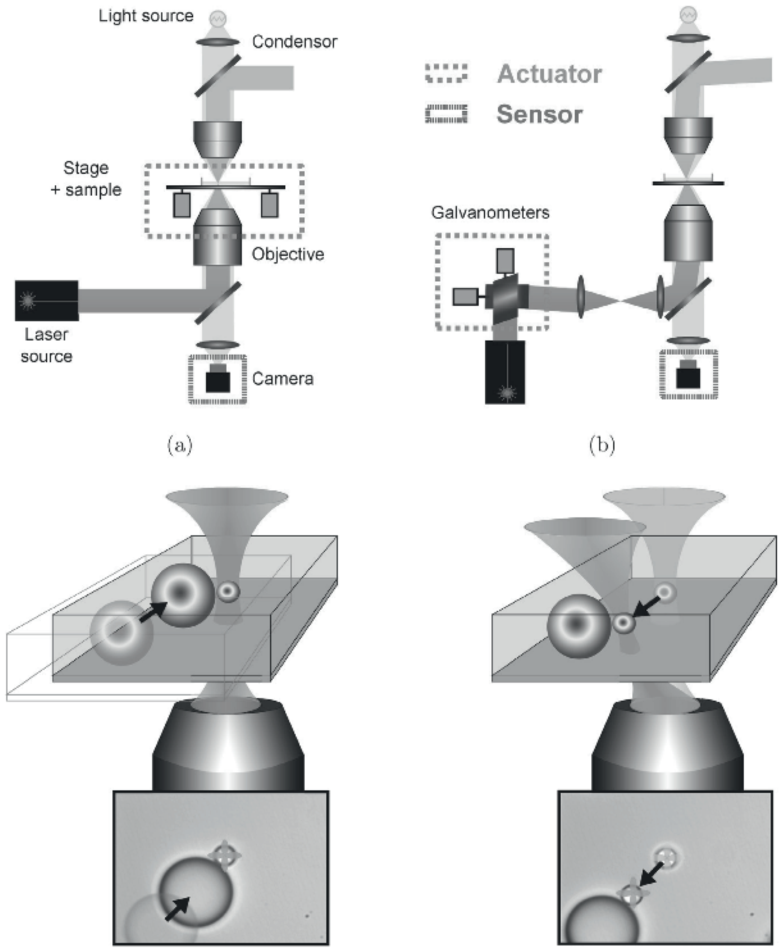


Figure 1.3. *Comparison of two actuation techniques. a) Conventional design for a single trap: the actuator is a motorized stage and the force sensor is a camera. b) Modification of OT setup with a deflective actuator (galvanometers). Schematic representation of the impact of the two different actuation methods on the sample and the microscope camera for c) stage-based and d) deflective methods. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

The deflection technique uses special devices to change the laser direction from the light path. A small angle deviation of a lens or a mirror on the laser path shifts the beam trajectory from the optical axis of the experimental setup. The laser is then guided by a telescope to the objective aperture. This deflection angle is used to displace the laser spot on the sample plane (see Figures 1.3(c) and (d)). When the deflection is achieved by a system with low inertia, the actuation is very fast, with response times down to 1 s [VIS 96, RUH 11]. Many methods exist for optical deflection [SVO 94, NEU 04], and Figures 1.4 (b) to (f) present the optical schemes of the available techniques for high-speed positioning. Table 1.2 summarizes the performances of different available components (in 2012).

The cheapest of the fast actuators (> 1 kHz, see Table 1.2) are the galvanometers, i.e. tiny mechanical motors with high resonance frequency (< 10 kHz). These deflectors are used in several OT setups and, in particular, for advanced control schemes [VIS 98, SPE 09]. Several experimental setups using piezoelectric mirror scanners promise good results for small deflection angles [MIO 00]. Three-dimensional positioning is possible with an additional Z-axis piezoelectric scanner which is fixed on a mirror or a lens on the light path [ARA 06]. Parallel trapping of multiple objects is possible with a single laser by temporal separation of the laser power [SAS 91].

The quickest actuators are presently the acousto-optical deflectors (AOD) [NAM 02] (see Table 1.2 for performance details), where acoustic standing waves in a crystal are used as a diffractive grating. This phenomenon creates interferences of different orders. As only the most intense beam (1st order) is isolated, power losses are significant ($> 30\%$); however, speed performances are excellent with more than 1 GHz bandwidth [VIS 96, RUH 11].

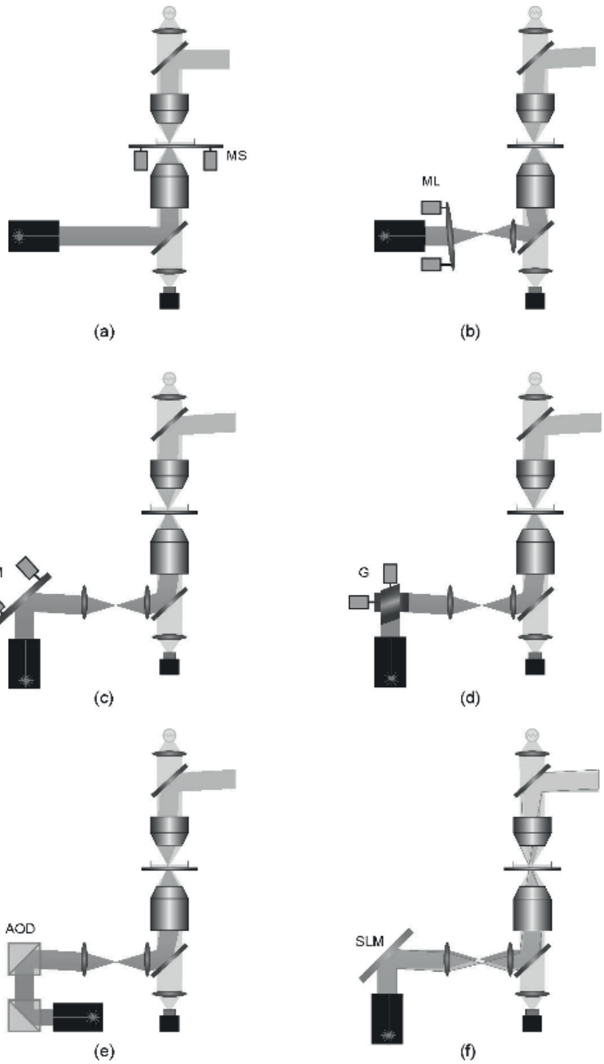


Figure 1.4. *Different actuators used in optical tweezers. a) Motorized stage (MS), b) piezo-motorized lens (PML), c) piezo-motorized mirror (PMM), d) galvanometers (G), e) acousto-optical deflector (AOD) and f) spatial light modulator (SLM). For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

A different approach is proposed by holographic techniques. Special liquid crystal devices (LCDs), named spatial light modulators (SLMs) [DUF 01, GRI 03], allow phase modulation of the laser light. The resulting interference patterns create several spatially addressable spots [CUR 02, GAR 02]. The usual frame refreshment rate, i.e. sampling rate, is 60 Hz following the typical LCD frequency. However, new SLM techniques achieve better speed performances (>200 Hz [PRE 09, HOS 03]). The particularity of those devices is the spatial sharing of the laser power which allows more than 200 independent optical traps and therefore collaborative operations of microtools [GRI 09]. SLMs are also the most convenient techniques to achieve 3D displacement (see Table 1.2).

Actuation of optical traps by deflection of the laser is efficient and elegant, but has the downside of changing the alignment between the optical axis and the sensors. New strategies for force measurements must be developed to deal with the properties of reflective or interferometric deflection phenomena.

1.3.2. *Impact of the laser deflection*

To our knowledge, advanced experimental setups for simultaneous actuation and measurement only allow steering within a workspace of less than 10 μm [VIS 98, RUH 11]. This small working domain is due to laser misalignment induced by the deflection.

At this stage, it is useful to recall the measurement principle of OTs [NEU 04, SVO 94]. A tiny focusing of the Gaussian laser is achieved by using a high with a high numerical aperture microscope objective. In this configuration, the resulting electromagnetic field induces optical forces on objects within the focus. In the microscaled case in particular, these interactions are well known on the spherical dielectric object: the force can be compared to the action of a linear 3D spring around a central equilibrium position, i.e. the laser focus [ASH 92, ROH 05b] (see Figure 1.2(c)). The proportional factor between the optical forces, F_{opt}, and the relative position of a microsphere, $X_{sphere} - X_{laser}$, is then defined as the trap stiffness, K, within the OT linear domain:

$$F_{opt} = -K \times (X_{sphere} - X_{laser}). \quad [1.1]$$

Moreover, due to the overdamped dynamics in microscale aqueous environments, inertial factors become negligible compared to viscous effects (low Reynolds flow [HAP 73]). The force balance can be considered as a static equation:

$$0 \approx F_{others} + F_{opt}. \quad [1.2]$$

The interaction of this microspherical probe, F_{others}, with its surroundings can then be estimated from the position measurement. This interesting property provides a simple and reliable indirect method for force measurement.

$$F_{others} = -F_{opt} = K \times (X_{sphere} - X_{laser}) = K \times X_{sphere/laser}. \quad [1.3]$$

The position measurement is obtained by an image projection of the trapped object (or the laser interferences) on the sensor, centered on the optical axis. A laser misalignment with the optical axis directly impacts the projection on the sensors and may cause the working domain to shrink or disappear. How to obtain a precise measurement of relative position ($X_{sphere/laser}$) over a large domain is a subtle question which requires further discussion.

1.3.3. *Measurement techniques*

For a good spatial resolution, the direct measurement of the relative position $X_{sphere/laser}$ between laser and the trapped bead is achieved with only one sensor instead of carrying out two separate measurements of the laser and bead positions. This purpose is easily achieved with special optical systems (see Figure 1.5).

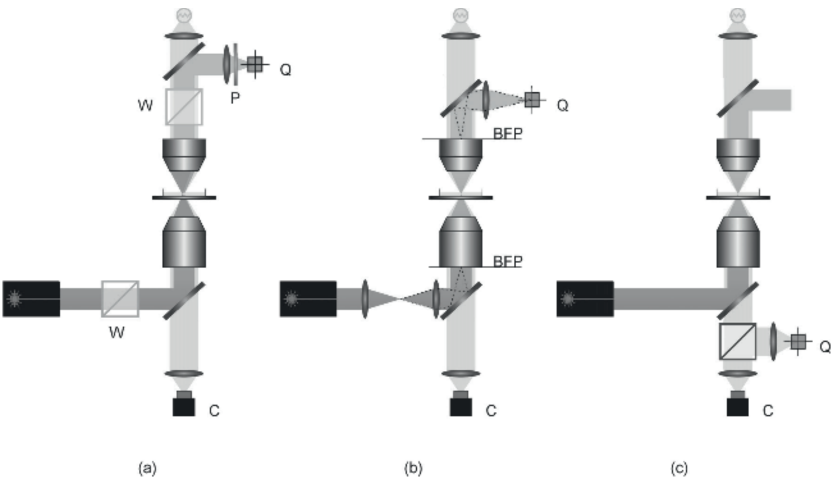


Figure 1.5. *Position detection techniques for optical force measurement. a) Interferometer using Wollaston prisms (W), a polarizer (P) and a quadrant photodiode (Q). b) Technique using back focal plane (BFP) interferences of the condenser. c) Imaging technique with quadrant or camera (C). For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

The first scheme, using differential position measurement (see Figure 1.5.(a)), is based on differential interference contrast microscopy: two Wollaston prisms split the trapping laser beam slightly before the sample plane and then combine it again after the sample plane. Two imperceptibly separated beam paths are created near the optical trap. Any disturbance of the trapped object position unbalances the two paths and produces a resulting phase shift on the photodiode sensors. This information is directly correlated to the desired relative position [DEN 90, SVO 93]. Moreover, this interferometric phenomenon has a very good spatial resolution since it is not limited by the laser wavelength. Unfortunately, the optical path only provides a one-dimensional measurement and is very sensitive to mechanical noise. The interferometric optics cost and alignment complexity explain why it is barely used now. Other interferometric and alternative techniques are detailed in Table 1.3.

The second interferometric cited method, named "back focal plane" (BFP), gives good 3D results for small particles (compared to the laser wavelength). In this case, the scattered part of the laser beam, going through the bead, interferes with the unscattered part [ROH 02]. The interference pattern is imaged on the condenser [VIS 98, GIT 98] or the objective [PRA 99] BFP (see Figure 1.5.(b)). The correlation between the signal and the relative position is well known and a simple quadrant photodiode is sufficient for 3D measurement [ROH 02]. Furthermore, telescope optical schemes reduce the sensitivity to trap misalignment (workspace $\approx$ 5 [VIS 96] to 10 μm [RUH 11]). This configuration gives good results for closed-loop control and artificial trap stiffness tuning [VIS 98, WUL 07]. It is also used in metrological workbenches, called photonic force microscopes [ROH 02, ROH 04].

	MS	PS	G	PMM/PML	AOD	SLM
Model	M-126.DG1 (x3)	P-563.3CD XYZ	6200H	S325	DTSXY	PLUTO
Supplier	PI	PI	CT	PI	QT	Holoeye
Dim	3D	3D	2D	3D (Z,θ_x,θ_y)	2D	3D
Multi-trap	No	No	Temporal	Temporal	Temporal	Spatial
Beam diameter	–	–	7 mm	25 mm	6.7 mm	8 mm
Bandwidth (kHz)	<0.005	< 0.015	<10	1–2	< 30,000	0.060
Spatial resolution	100 nm	0.5 nm	8 μrds	0.1 μrds	25 μrds	$1,920\times1,080$
Maximal range	25 mm	300 μm	$\pm$350 $mrds$	$\pm$30 μm, 4 $mrds$	$\pm$26 $mrds$	100μm
Optical loss	0	0	$<$ 3 %	$<$ 3 %	$>$ 40 %	40 %
Price estimation	€€	€€€€	€	€	€€	€€€€

Table 1.2. *Comparison of usual optical tweezers actuators according to the supplier's data sheets. Abbreviations: MS: motorized stage; PS: piezoelectric stage; G: galvanometer; PMM / PML: mirror or lens mount on a piezoelectric scanner; AOD: acousto-optical deflectors; SLM: spatial light modulator; PI: Physik Instrument; CT: Cambridge Technology; QT: QUANTA TECH*

Techniques	References	Diameter	Price (K€)	Illumination	Acquisition	Image processing	Algorithm
Interferometer	[DEN 90]	1D	€€€€	Laser	100 kHz	–	–
Back focal plane	[ROH 02]	3D	€	Laser	850 kHz	–	–
Photodiode imaging	[SIM 96]	2D	€	Tungsten 100 W	2 kHz	–	–
Fast CMOS	[KEE 07]	2D	€€	Halogen 100 W	2 kfps	Offline	–
Fast CMOS	[GIB 08]	2D	€€	Halogen 50 W	2 kfps	0.5 kHz	Centroid
FPGA	[OTT 10]	2D	€€	Cold LED 15 W and optical fiber	10 kfps	10 kHz	Hardware
Stereoscopy	[BOW 10]	3D	€€	2 × white LED 3 W and optical fiber	340 Hz	340 Hz	Symmetry recognition
DVS	[NI 11]	2D	€€	Cold LED 5W	3 kHz	30 kHz	Spare matrix Hough circle

Table 1.3. *Comparison of high-speed position detection methods. The acquisition and image processing are in frames per second (fps) for cameras and refreshing rate (Hz) for others*

However, the two previous solutions are difficult to implement and a simpler scheme is often preferred: object imaging with a white light source [CRO 96] or an additional laser beam [SIM 96]. This technique is suitable only for big visible objects under an optical microscope to preserve an adequate resolution. The image is commonly acquired with two types of sensor: quadrant photodiode or video cameras. Quadrant photodiodes were the first position detectors. As these sensors only have four pixels, their acquisition rate is high (>1 GHz [SPE 09]). Higher resolution image sensors facilitate useful image processing metrics obtained with algorithms such as centroids, histograms, interpolation and cross-correlation [CRO 96, CHE 01, CAR 05]. Information obtained by their numerous pixels is highly valuable to discriminate shapes, impurities and contacts [UEB 12]. Sensor alignment is facilitated by software reallocation of the region of interest (ROI), and image data also lead to fine-tuning of focus via edge sharpness.

Today, new generations of complementary metal-oxide semiconductor (CMOS) cameras allow more than 2,000 frames per second for a reduced ROI [KEE 07, OTT 10]. For the purpose of OTs, this is sufficient [KEE 07, GIB 08] because the relaxation time of the OT phenomena is limited in an aqueous medium by fluid viscosity and trap stiffness; existing system bandwidth is therefore often below 1 kHz. Despite the fact that acquisition time is not an issue, computing resources are still not able to achieve complex and robust image processing at this rate [CHE 01, UEB 12]. For example, a centroid calculation can be very fast (performed at more than 10 kHz) but it is very sensitive to disturbances such as shadows, contacts and impurities, and therefore does not provide a reliable and safe force measurement with random experimental conditions. In comparison, the Hough transform [ILL 88, SME 08] is very robust to track spherical objects, but it is highly time-consuming and so, in this case, not practical. Recent development of vision sensors encourages new high-speed tracking techniques. Field-programmable gate arrays (FPGA) or smart cameras are used to perform embedded hardware image processing and this allows refresh rates of the position information up to 10 kHz [TOW 09, SIL 11] and for two simultaneous bead trackings [IKI 09]. A new sensor, asynchronous temporal contrast silicon retina dynamic vision sensors (DVS), provides event-based information of the scene and records only intensity changes [LIC 08, NI 11, DRA 11]. It allows software solutions for dynamic event processing at more than 30 kHz [NI 11]. It is important to note that at such high acquisition rates, the temporal resolution meets limitations due to the number of photons which can reach the sensors during the acquisition period. Illumination with a higher light power is necessary [OTT 10, BIA 06].

In summary, existing systems do not satisfy the necessary conditions for good force feedback operations, especially the workspace size and system bandwidth. The recent technologies and their future developments are promising directions to investigate for better teleoperated optical tweezer performances.

1.4. Specific designs for haptic interactions

Performance of teleoperated manipulators depends on the latency and speed of the interface dynamics, adequate degrees of freedom for the manipulation required, and adequate resolution and amplitude of force to mimic normal human interaction with directly tangible objects. The existing optical path designs of OT are insufficient and a new design is needed. There are few existing propositions worth discussing.

To achieve multiple traps or degrees of freedom, a laser beam may be separated into multiple traps by division in time or space. In temporally divided trapping, multiple traps are sequentially illuminated at a faster rate than the trapped object's natural dynamics. In spatially divided trapping, multiple traps can be formed by shaping the laser with grating or holographic interometric methods. Furthermore, many groups [WHY 06, GRI 09, OND 12a] are looking for collaborative haptic micromanipulation systems (for instance, with two hands or two users) using these two methods.

1.4.1. *Temporal sharing*

For fast scanning techniques, new optical schemes must be proposed to overcome the misalignment issues. We illustrate this argument with an example from Padgett's team and collaborators [PAC 09]. As Figure 1.6 shows, placing the sensor on the other side of the deflective actuator is an easy way to solve the issue. In this manner, the white light reaches and goes through the actuator in the exact opposite direction from the laser beam. Doing so, the image on the sensor is always centered on the laser spot. However, the actuator must have special optical properties: it reflects or transmits light with few aberrations and indifferently from one side or the other. In other words, it is an optically reversible deflector. Galvanometers are well suited for this purpose [PAC 10], while AOD (see section 1.3.1) or SLM are not convenient because of the use of interference patterns.

Using this method, meaningful sensations have been perceived. In work by Padgett's team and collaborators [PAC 09], shape explorations have been achieved with microprobes (see Figure 1.7). The edge of a silica microelectromechanical systems (MEMS) corner is perfectly tactually recognizable. Other sensations such as viscous drag and Brownian motion are reliably fed back to the user. In terms of performance, the workspace is now unlimited in the microscope view.

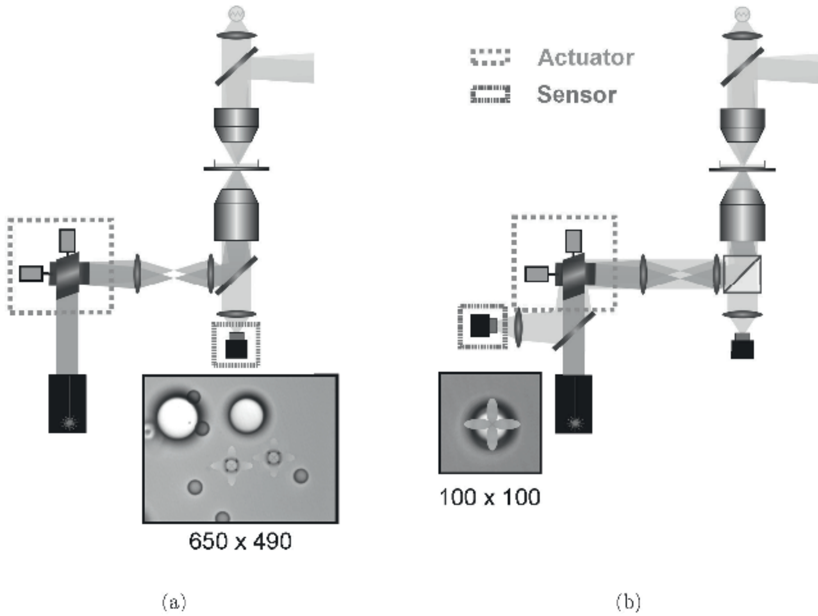
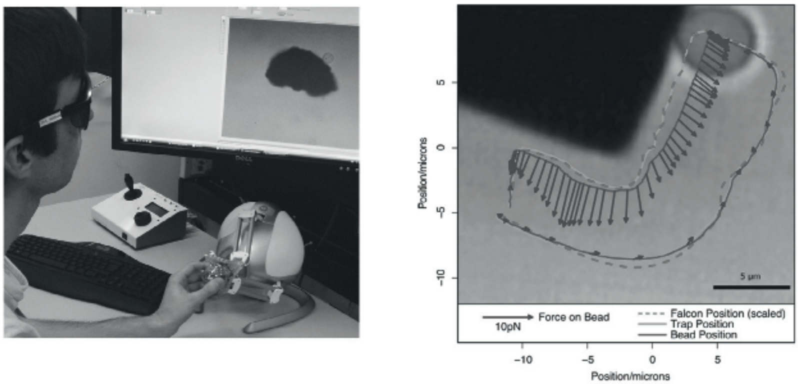


Figure 1.6. *Backward and forward imaging principle. a) The image is obtained at the back of the actuator on the laser path and b) the image is obtained in front of the actuator and stays aligned with the laser deflection. The image area can be reduced to decrease acquisition and processing times. The actuator, here galvanometers, should be reversible, i.e. reflective or transmissive in both ways. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

With this configuration, the dynamics and bandwidth are good enough for one trap. For several traps, the power must be temporally shared, and the scan frequency must be high enough so that each trap is updated faster than its natural physical dynamics, i.e. the trapped particle does not notice the discontinuity. In the case of the time sharing technique, only one sensor receives the measurement of all the scanned points. The synchronization between the acquisition time and the standing time of the scanner is just a technical issue. This has already been performed with ultra high-speed sensors for nine traps [RUH 11] without any haptic purpose. The remaining issue to achieve our goal is to find the adequate sensors and processing power for fast and robust measurement.



(a) (b)

Figure 1.7. *Results with the forward imaging technique. a) Operator during an exploration. b) Haptic feedback rounds the corner of a silica cubic MEMS (Extract from [PAC 09]). For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

1.4.2. *Spatial sharing*

Galvanometers, however, provide only 2D actuation capabilities. For 3D multi-contact grasping, holographic systems such as SLM are more elegant. Recent works show an implementation of holographic optical tweezers (HOTs) with two force feedback handles [OND 12a]. This system uses an enhanced nematic liquid crystal SLM and a fast CMOS camera. The haptic coupling loop rate is only 100 Hz (instead of the recommended 1 kHz) because of SLM and image processing limitations. Moreover, the choice of actuators and command produces a significant delay between the user handle motion and the actual laser actuation. This leads to insufficient amplitude of the force feedback due to system instabilities.

Nowadays, faster SLM devices are available [HOS 03]. Ferroelectric SLMs can create hologram patterns at up to 1,440 Hz. Few implementations have proved the efficiency of this technology up to 1 kHz [PRE 09, BOW 11a, THA 13]. The high cost of these components puts off some laboratories. Assuming the fast SLM technologies available, specific force measurement techniques should be developed.

In this case, the trapped objects travel in a large area and cannot be tracked with the previous specific optical methods (BFP or backward imaging camera, see Figure 1.6). This reduces the acquisition and processing speed, or the resolution. For example, one of the best propositions comes from Bowman *et al*. [BOW 11a]. The symmetric properties of the probes that are used are higher level algorithms than a centroid, on the 60×60 pixels of the CMOS and succeeded with having a force refreshing rate of 400 Hz.

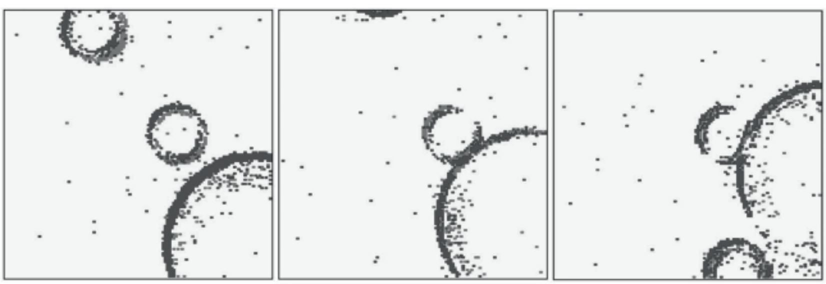


Figure 1.8. *Dynamic image of two microspheres (*3 *μm and* 11 *μm) put into contact. Dots are the events sent by the asynchronous pixels in a 30 ms time window. The color of the dots depends on the increment or decrement of light intensity on pixels. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

The bottleneck between fast refresh and high-level detection, which are robust to external disturbance, can be solved today by new sensor technologies. For example, the asynchronous retina has a real advantage for increasing precision and speed of force measurements. Sensitive to intensity changes, the desynchronized pixels provide only the useful information about the scene and act as an edge detector [NI 11] (see Figure 1.8). Pixel events are sent as a continuous flow addressed by hardware time stamps and location. The commercially available sensors have 1 μs clock resolution for 128×128 pixels and each pixel has a 3 kHz bandwidth [LIC 08]. Specific image processing is performed on an event list which may be seen as a sparse matrix. Highly complex algorithms are implemented with incomparably high speed and low computational resources. Efficient tracking of multiple microspheres with Hough transform methods within 100 μs are performed. As these sensors are in an early state of development, their potential for better pixel resolution, bandwidth and contrast ratio promises even larger improvement of microscopy applications. For example, some ongoing works are focused on multi-trapping, out-of-focus measurements and better haptic sensations [NI 13] (higher resolution, stability and reliability).

1.5. Discussion

Looking at these recent developments, interactive micromanipulators have never been so close to the human hand. A few experimental setups have already displayed reliable and useful feedback [PAC 09, PAC 10, BOW 11a, NI 13]. However, more research must be conducted to obtain the full potential of this method. The most important aspects are discussed in this section: z-axis force feedback, stiffness model limitations, advanced trap microtools and haptic devices.

The trap stiffness is lower along the z-axis and, as a result, beads escape frequently [DIE 11]. The depth of field of the microscope image (with high numerical aperture objectives <1 μm) is narrow, i.e. objects become blurred when travelling on the z-axis. This out-of-focus effect explains why z-axis particle tracking is more difficult than in the x- and y-axis in microscopy. For small particles, BFP techniques are very efficient due to laser interferences dependence on z-axis displacement [ROH 04]. However, this measurement is not robust to external disturbances (obstacles, impurities, etc.). For objects bigger than laser wavelength, other techniques exist, such as image processing of the diffraction pattern of the trapped object [ZHA 08b, CHE 09]. Another option is to obtain a stereoscopic image with two different light sources [DAM 08, BOW 10]: the distance between the two projected images of an object is used to determine the relative axial position of the trapped object. Tiny displacements are hence magnified, but the image acquisition and processing must be performed on a larger area. Three-dimensional images are also obtained by holographic techniques based on the light phase. Custom digital holographic microscopes are under development [SHE 06, CHE 10]. More research must be carried out to propose a satisfactory temporal bandwidth of sensors, algorithms and imaging sources.

Quantitative force measurement is a delicate subject because it is based on a model with numerous limitations. OT has proven metrologic capacities [ROH 05a] in a controlled environment. The linear trap stiffness model is only accurate away from obstacles [ASH 92]. Real interactions bring other issues: uncontrolled environments, impurities, lateral or axial contacts, and particle overlap. In these conditions, the laser is modified by surrounding objects and the optical force model is no longer accurate. More research must be carried out on models for contact conditions and on the influence of impurities. However, because human tactile perception of force is relative, a precise and quantitative value of the force is not necessary for haptics, but disturbances should not alter the sensations while operating.

Different laboratories are developing advanced robot-like microtools, which can benefit from a haptic force feedback. These new properties benefit from special materials, such as gels [MAR 07] and photopolymerized structures [DAM 08], and from custom structures with several trapping sites [PAL 13, FUK 12, PHI 11, IKI 09]. Therefore, these microtools possess a complex balance of force while interacting with the sample. Force models and measurements are being investigated [PHI 11, CAR 10]. These structures are complex to control: additional degrees of freedom like rotation, parallel traps, rigid or flexible parts. These parameters can be processed by advanced and intuitive interfaces that can merge position and force information in the user's hand (see Figure 1.9).

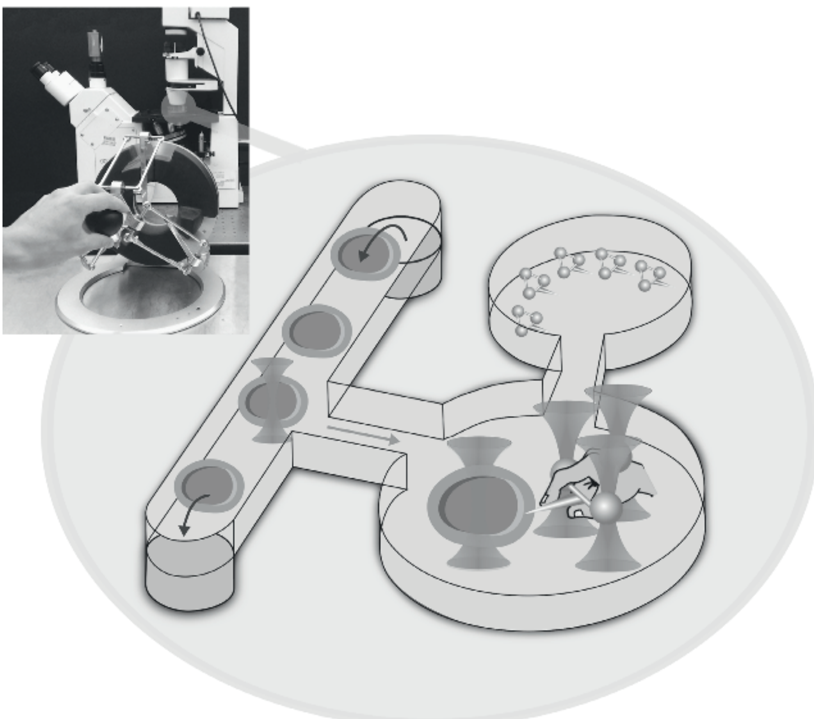


Figure 1.9. *Concept of advanced nimble microtools to explore cells using optical tweezers and haptic force feedback. For a color version of this figure, see www.iste.co.uk/ni/tweezers.zip*

The master interface system and operator mechanics are interlinked with the slave (micromanipulator) system. Further improvements must be proposed on both sides of the haptic coupling loop to be worth increasing the performance. First, the mechanical bandwidth of commercial haptic interfaces is particularly unsatisfactory and adds instabilities in the haptic coupling loop [ABB 05, MOH 12]. The second important issue is the inadequacy of existing designs for the specific tasks of micromanipulation: handle shapes, degrees of freedom, and structure are not intuitive for the tasks and collaborative works. Therefore, commercial haptic devices are no longer the optimal choice for the master side, and the micromanipulation community must collaborate with the haptic community to conceive new designs for their specific applications [MOH 12, VEN 10, EST 10].

1.6. Conclusion

This first chapter summarized the essential points for the construction of an efficient haptic feedback micromanpulation platform. The main idea is to consider the haptic optical tweezers as a whole, instead of the combination of two systems. The chapter also highlights requirements in terms of bandwidth, workspace and robustness for the complete system.

As human perception of force amplitude is not quantitative and precise, force feedback teleoperation is an efficient solution to display helpful qualitative information of microworld explorations. In our case, the amplitude resolution of the force measurement is a less important specification than the temporal resolution and robustness to disturbances because the feedback must be safe and useful.

All things considered, more research and effort are still required to obtain a practical and useful haptic feedback platform. This chapter proposes new leads and sheds light on the latest interesting topics for the research community. It also defines new standards and specifications for commercial systems that want to benefit from fully intuitive and dexterous platforms.

The potential of this method is huge, particularly in the field of biomedicine where optical tweezers are used on a large scale. The force feedback can reduce the time of operations and increase the feasible complexity of tasks. The new capabilities offered by haptic optical tweezers will inspire future studies and the diagnosis of new types of cells [DIF 13, ESS 12] or facilitate complex assembly of biomedical materials [GON 12].

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